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☐	L6	l4 and ((amino acid$) adj3 (synthe$ or (non adj (native or natur$))))	2
☐	L5	L4 and aminoacyl$	4
☐	L4	l2 with (link$ or bound$ or bind$ or conjug$ or tether or attach$) with L3	81
☐	L3	(enzymati$ nucle$ acid$) or (catalyt$ RNA) or (enzymat$ RNA) or (catalytic DNA) or (enzymat$ nuclei$ acid) or ribozym$ or (catalyt$ oligonucleoti$) or nucleozym$ or DNAzyme or (RNA enzyme) or (endoribonucleas$) or endonuclease$ or oligozyme or (DNA enzyme)	41529
☐	L2	trna$	12796
☐	L1	5792613.pn.	2

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NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS	4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS	5	FEB 05	German (DE) application and patent publication number format changes
NEWS	6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS	7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	8	MAR 03	FRANCEPAT now available on STN
NEWS	9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS	10	MAR 29	WPIFV now available on STN
NEWS	11	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS	12	APR 26	PROMT: New display field available
NEWS	13	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS	14	APR 26	LITALERT now available on STN
NEWS	15	APR 27	NLDB: New search and display fields available
NEWS	16	May 10	PROUSDDR now available on STN
NEWS	17	May 19	PROUSDDR: One FREE connect hour, per account, in both May and June 2004
NEWS	18	May 12	EXTEND option available in structure searching
NEWS	19	May 12	Polymer links for the POLYLINK command completed in REGISTRY

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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=> FIL MEDLINE BIOSIS EMBASE CA SCISEARCH
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                                                      ENTRY     SESSION
FULL ESTIMATED COST                                    0.21        0.21

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=> s trna?
L1        92137 TRNA?

=> s (enzymati? nucle? acid?) or (catalyt? RNA) or (enzymat? RNA) or (catalytic
DNA) or (enzymat? nuclei? acid) or ribozym? or (catalyt? oligonucleoti?) or
nucleozym? or DNAzyme or (RNA enzyme) or (endoribonucleas?) or endonuclease? or
oligozyme or (DNA enzyme)
   3 FILES SEARCHED...
L2       139414 (ENZYMATI? NUCLE? ACID?) OR (CATALYT? RNA) OR (ENZYMAT? RNA) OR
                (CATALYTIC DNA) OR (ENZYMAT? NUCLEI? ACID) OR RIBOZYM? OR (CATAL
                YT? OLIGONUCLEOTI?) OR NUCLEOZYM? OR DNAZYME OR (RNA ENZYME) OR
                (ENDORIBONUCLEAS?) OR ENDONUCLEASE? OR OLIGOZYME OR (DNA ENZYME)


=> s l1 (s) (link or bound or bind or conjug or tether or attach) (s) l2
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=> s l1 (s) (link? or bound? or bind? or conjug? or tether? or attach?) (s) l2
L3          463 L1 (S) (LINK? OR BOUND? OR BIND? OR CONJUG? OR TETHER? OR ATTACH
                ?) (S) L2

=> s l3 and aminoacyl?
L4           40 L3 AND AMINOACYL?

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5           22 DUP REM L4 (18 DUPLICATES REMOVED)

=> s l5 and py<=2000
   2 FILES SEARCHED...
   4 FILES SEARCHED...
L6           11 L5 AND PY<=2000

=> d l6 1-11 ibib abs

L6   ANSWER 1 OF 11     MEDLINE on STN
ACCESSION NUMBER:    92294868     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 1604316
TITLE:               Aminoacyl esterase activity of the Tetrahymena
```

ribozyme.

COMMENT: Comment in: Science. 1992 Jun 5;256(5062):1396-7. PubMed ID: 1376495
Comment in: Science. 1992 Jun 5;256(5062):1402-3. PubMed ID: 1376496

AUTHOR: Piccirilli J A; McConnell T S; Zaug A J; Noller H F; Cech T R

CORPORATE SOURCE: Howard Hughes Medical Institute, Department of Chemistry and Biochemistry, University of Colorado, Boulder 80309.

SOURCE: Science, **(1992 Jun 5)** 256 (5062) 1420-4.
Journal code: 0404511. ISSN: 0036-8075.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199207
ENTRY DATE: Entered STN: 19920724
Last Updated on STN: 19970203
Entered Medline: 19920715

AB Several classes of ribozymes (catalytic RNA's) catalyze reactions at phosphorus centers, but apparently no reaction at a carbon center has been demonstrated. The active site of the Tetrahymena **ribozyme** was engineered to **bind** an oligonucleotide derived from the 3' end of N-formyl-methionyl-**tRNA**(fMet). This ribozyme catalyzes the hydrolysis of the **aminoacyl** ester bond to a modest extent, 5 to 15 times greater than the uncatalyzed rate. Catalysis involves binding of the oligonucleotide to the internal guide sequence of the ribozyme and requires Mg2+ and sequence elements of the catalytic core. The ability of RNA to catalyze reactions with **aminoacyl** esters expands the catalytic versatility of RNA and suggests that the first **aminoacyl** tRNA synthetase could have been an RNA molecule.

L6 ANSWER 2 OF 11 EMBASE
on STN

ACCESSION NUMBER: 2000386860 EMBASE

TITLE: Correlating amino acid conservation with function in tyrosyl-tRNA synthetase.

AUTHOR: Xin Y.; Li W.; Dwyer D.S.; First E.A.

CORPORATE SOURCE: E.A. First, Dept. of Biochem./Molecular Biol., Louisiana State University, Health Sciences Center, Shreveport, LA 71130, United States. efirst@lsuhsc.edu

SOURCE: Journal of Molecular Biology, (20 Oct 2000) 303/2 (287-298).
Refs: 70
ISSN: 0022-2836 CODEN: JMOBAK

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Sequence comparisons have been combined with mutational and kinetic analyses to elucidate how the catalytic mechanism of Bacillus stearothermophilus tyrosyl-**tRNA** synthetase evolved. Catalysis of **tRNA**(Tyr) **aminoacylation** by tyrosyl-**tRNA** synthetase involves two steps: activation of the tyrosine substrate by ATP to form an enzyme-**bound** tyrosyl-adenylate intermediate, and transfer of tyrosine from the tyrosyl-adenylate intermediate to **tRNA**(Tyr). Previous investigations indicate that the class I conserved KMSKS motif is involved in only the first step of the reaction (i.e. tyrosine activation). Here, we demonstrate that the class I conserved HIGH motif also is involved only in the tyrosine activation step. In contrast, one amino acid that is conserved in a subset of the class I **aminoacyl**-**tRNA** synthetases, Thr40, and two

amino acids that are present only in tyrosyl-**tRNA** synthetases, Lys82 and Arg86, stabilize the transition states for both steps of the **tRNA aminoacylation** reaction. These results imply that stabilization of the transition state for the first step of the reaction by the class I **aminoacyl-tRNA** synthetases preceded stabilization of the transition state for the second step of the reaction. This is consistent with the hypothesis that the ability of **aminoacyl-tRNA** synthetases to catalyze the activation of amino acids with ATP preceded their ability to catalyze **attachment** of the amino acid to the 3' end of **tRNA**. We propose that the primordial **aminoacyl-tRNA** synthetases replaced a **ribozyme** whose function was to promote the reaction of amino acids and other small molecules with ATP. (C) 2000 Academic Press.

L6 ANSWER 3 OF 11 EMBASE
on STN

ACCESSION NUMBER: 2000287480 EMBASE
TITLE: Effects of 5' leader and 3' trailer structures on pre-tRNA processing by nuclear RNase P.
AUTHOR: Ziehler W.A.; Day J.J.; Fierke C.A.; Engelke D.R.
CORPORATE SOURCE: D.R. Engelke, Dept. of Biol. Chem./Dept. of Chem., University of Michigan, Ann Arbor, MI 48109-0606, United States. Engelke@Umich.edu
SOURCE: Biochemistry, (15 Aug 2000) 39/32 (9909-9916).
Refs: 35
ISSN: 0006-2960 CODEN: BICHAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Eukaryotic transfer RNA precursors (pre-**tRNAs**) contain a 5' leader preceding the **aminoacyl** acceptor stem and a 3' trailer extending beyond this stem. An early step in pre-**tRNA** maturation is removal of the 5' leader by the **endoribonuclease**, RNase P. Extensive pairing between leader and trailer sequences has previously been demonstrated to block RNase P cleavage, suggesting that the 5' leader and 3' trailer sequences might need to be separated for the substrate to be recognized by the eukaryotic holoenzyme. To address whether the nuclear RNase P holoenzyme recognizes the 5' leader and 3' trailer sequences independently, interactions of RNase P with pre-**tRNA**(Tyr) containing either the 5' leader, the 3' trailer, or both were examined. Kinetic analysis revealed little effect of the 3' trailer or a long 5' leader on the catalytic rate (k(cat)) for cleavage using the various pre-**tRNA** derivatives. However, the presence of a 3' trailer that pairs with the 5' leader increases the K(m) of pre-**tRNA** slightly, in agreement with previous results. Similarly, competition studies demonstrate that removal of a complementary 3' trailer lowers the apparent K(I), consistent with the structure between these two sequences interfering with their interaction with the enzyme. Deletion of both the 5' and 3' extensions to give mature termini resulted in the least effective competitor. Further studies showed that the nuclear holoenzyme, but not the B. subtilis holoenzyme, had a high affinity for single-stranded RNA in the absence of **attached tRNA** structure. The data suggest that yeast nuclear RNase P contains a minimum of two **binding** sites involved in substrate recognition, one that interacts with **tRNA** and one that interacts with the 3' trailer. Furthermore, base pairing between the 5' leader and 3' trailer hinders recognition.

L6 ANSWER 4 OF 11 EMBASE
on STN

ACCESSION NUMBER: 1998206201 EMBASE

TITLE: Ribosomal proteins S5 and L6: High-resolution crystal structures and roles in protein synthesis and antibiotic resistance.
AUTHOR: Davies C.; Bussiere D.E.; Golden B.L.; Porter S.J.; Ramakrishnan V.; White S.W.
CORPORATE SOURCE: V. Ramakrishnan, Department of Biochemistry, University Utah School of Medicine, Salt Lake City, UT 84132, United States
SOURCE: Journal of Molecular Biology, (19 Jun 1998) 279/4 (873-888).
Refs: 88
ISSN: 0022-2836 CODEN: JMOBAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Antibiotic resistance is rapidly becoming a major medical problem. Many antibiotics are directed against bacterial ribosomes, and mutations within both the RNA and protein components can render them ineffective. It is well known that the majority of these antibiotics act by **binding** to the ribosomal RNA, and it is of interest to understand how mutations in the ribosomal proteins can produce resistance. Translational accuracy is one important target of antibiotics, and a number of ribosomal protein mutations in Escherichia coli are known to modulate the proofreading mechanism of the ribosome. Here we describe the high-resolution structures of two such ribosomal proteins and characterize these mutations. The S5 protein, from the small ribosomal unit, is associated with two types of mutations: those that reduce translational fidelity and others that produce resistance to the antibiotic spectinomycin. The L6 protein, from the large subunit, has mutations that cause resistance to several aminoglycoside antibiotics, notably gentamicin. in both proteins, the mutations occur within their putative RNA-**binding** sites. The L6 mutations are particularly drastic because they result in large deletions of an RNA-**binding** region. These results support the hypothesis that the mutations create local distortions of the **catalytic RNA** component. When combined with a variety of structural and biochemical data, these mutations also become important probes of the architecture and function of the translational machinery. We propose that the C-terminal half of S5, which contains the accuracy mutations, organizes RNA structures associated with the decoding region, and the N-terminal half, which contains the spectinomycin-resistance mutations, directly interacts with an RNA helix that **binds** this antibiotic. As regards L6, we suggest that the mutations indirectly affect proofreading by locally distorting the EF-Tu·GTP· **aminoacyl tRNA binding** site on the large subunit.

L6 ANSWER 5 OF 11 EMBASE
on STN
ACCESSION NUMBER: 97005230 EMBASE
DOCUMENT NUMBER: 1997005230
TITLE: A tyrosyl-tRNA synthetase recognizes a conserved tRNA-like structural motif in the group I intron catalytic core.
AUTHOR: Caprara M.G.; Lehnert V.; Lambowitz A.M.; Westhof E.
CORPORATE SOURCE: M.G. Caprara, Department of Molecular Genetics, Ohio State University, Columbus, OH 43210-1292, United States
SOURCE: Cell, (1996) 87/6 (1135-1145).
ISSN: 0092-8674 CODEN: CELLB5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology

LANGUAGE: English
SUMMARY LANGUAGE: English
AB The Neurospora crassa mitochondrial (mt) tyrosyl-**tRNA** synthetase (CYT- 18 protein) functions in splicing group I introns, in addition to **aminoacylating tRNA**(Tyr). Here, we compared the CYT-18 **binding** sites in the N. crassa mt LSU and ND1 introns with that in N. crassa mt **tRNA**(Tyr) by constructing three-dimensional models based on chemical modification and RNA footprinting data. Remarkably, superimposition of the CYT-18 **binding** sites in the model structures revealed an extended three-dimensional overlap between the **tRNA** and the group I intron catalytic core. Our results provide insight into how an RNA-splicing factor can evolve from a cellular RNA-**binding** protein. Further, the structural similarities between group I introns and **tRNAs** are consistent with an evolutionary relationship and suggest a general mechanism for the evolution of complex **catalytic RNAs**.

L6 ANSWER 6 OF 11 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 95102476 EMBASE
DOCUMENT NUMBER: 1995102476
TITLE: Minor groove recognition of the conserved G·U pair at the tetrahymena ribozyme reaction site.
AUTHOR: Strobel S.A.; Cech T.R.
CORPORATE SOURCE: Howard Hughes Medical institute, Department Chemistry Biochemistry, University of Colorado,Boulder, CO 80309-0215, United States
SOURCE: Science, (1995) 267/5198 (675-679). ISSN: 0036-8075 CODEN: SCIEAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The guanine.uracil (G·U) base pair that helps to define the 5'-splice site of group I introns is phylogenetically highly conserved. In such a wobble base pair, G makes two hydrogen bonds with U in a geometry shifted from that of a canonical Watson-Crick pair. The contribution made by individual functional groups of the G·U pair in the context of the Tetrahymena **ribozyme** was examined by replacement of the G·U pair with synthetic base pairs that maintain a wobble configuration, but that systematically alter functional groups in the major and minor grooves of the duplex. The substitutions demonstrate that the exocyclic amine of G, when presented on the minor groove surface by the wobble base pair conformation, contributes substantially (2 kilocalories mole-1 to **binding** by making a tertiary interaction with the **ribozyme** active site. It contributes additionally to transition state stabilization. The **ribozyme** active site also makes tertiary contacts with a tripod of 2'-hydroxyls on the minor groove surface of the splice site helix. This suggests that the **ribozyme** **binds** the duplex primarily in the minor groove. The alanyl **aminoacyl** transfer RNA (**tRNA**) synthetase recognizes the exocyclic amine of an invariant G·U pair and contacts a similar array of 2'-hydroxyls when **binding** the **tRNA**(Ala) acceptor stem, providing an unanticipated parallel between protein-RNA and RNA-RNA interactions.

L6 ANSWER 7 OF 11 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 95030564 EMBASE
DOCUMENT NUMBER: 1995030564
TITLE: **Aminoacyl**-tRNA synthetase and U54 methyltransferase recognize conformations of the yeast

tRNA(Phe) anticodon and T stem/loop domain.

AUTHOR: Guenther R.H.; Bakal R.S.; Forrest B.; Chen Y.; Sengupta R.; Nawrot B.; Sochacka E.; Jankowska J.; Kraszewski A.; Malkiewicz A.; Agris P.F.

CORPORATE SOURCE: Department of Biochemistry, North Carolina State University,Raleigh, NC 27695-7622, United States

SOURCE: Biochimie, (1994) 76/12 (1143-1151).
ISSN: 0300-9084 CODEN: BICMBE

COUNTRY: France

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The enyzme-catalyzed posttranscriptional modification of **tRNA** and the contributions of modified nucleosides to **tRNA** structure and function can be investigated with chemically synthesized domains of the **tRNA** molecule. Heptadecamer RNAs with and without modified nucleosides and DNAs designed as analogs to the anticodon and T stem/loop domains of yeast **tRNA**(Phe) were produced by automated chemical synthesis. The unmodified T stem/loop domain of Yeast **tRNA**(Phe) was a substrate for the E coli m5U54-**tRNA** methyltransferase activity, RUMT. Surprisingly, the DNA analog of the T stem/loop domain composed of d(A,U,G,C) was also a substrate. In addition, the DNA analog inhibited the methylation of unfractionated, undermodified E coli **tRNA** lacking the U54 methylation. RNA anticodon domains and DNA analogs differentially and specifically affected **aminoacylation** of the wild type yeast **tRNA**(Phe). Three differentially modified **tRNA**(Phe) anticodon domains with Ψ39 alone, m1G37 and m5C40, or Ψ39 with m1G37 and m5C40, stimulated phenylalanyl- **tRNA** synthetase (FRS) activity. However, one anticodon domain, with m5C40 as the only modified nucleoside and a closed loop conformation, inhibited FRS activity. Modified and unmodified DNA analogs of the anticodon, tDNA(Phe)(AC) inhibited FRS activity. Analysis of the enzyme activity in the presence of the DNA analog characterized the **DNA**/**enzyme** interaction as either partial or allosteric inhibition. The disparity of action between the DNA and RNA hairpins provides new insight into the potential allosteric relationship of anticodon **binding** and open loop conformational requirements for active site function of FRS and other aaRSs. The comparison of the stimulatory and inhibitory properties of variously modified RNA domains and DNA analogs demonstrates that conformation, in addition to primary sequence, is important for **tRNA**-protein interaction. The enzyme recognition of various DNA analogs as substrate and/or inhibitors of activity demonstrates that conformational determinants are not restricted to ribose and the standard A-form RNA structure.

L6 ANSWER 8 OF 11 EMBASE
on STN

ACCESSION NUMBER: 94167286 EMBASE

DOCUMENT NUMBER: 1994167286

TITLE: Three-dimensional working model of M1 RNA, the catalytic RNA subunit of ribonuclease P from Escherichia coli.

AUTHOR: Westhof E.; Altman S.

CORPORATE SOURCE: CNRS, Inst. de Biologie Molec./Cellulaire, 15 rue Rene Descartes,67084 Strasbourg-Cedex, France

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1994) 91/11 (5133-5137).
ISSN: 0027-8424 CODEN: PNASA6

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry

LANGUAGE: English
SUMMARY LANGUAGE: English
AB A three-dimensional model of M1 RNA, the **catalytic RNA** subunit of RNase P from Escherichia coli, was constructed with the aid of a computer. The modeling process took into account data from chemical and enzymatic protection experiments, phylogenetic analysis, studies of the activities of mutants, and the kinetics of reactions catalyzed by the **binding** of substrate to M1 RNA. The model provides a plausible picture of the **binding** to M1 RNA of the **tRNA** domain of a precursor **tRNA** substrate. The scissile bond and adjacent segments of the **aminoacyl** acceptor stem of a precursor **tRNA** substrate can fit into a cleft that leads to the phylogenetically conserved, central part of the structure.

L6 ANSWER 9 OF 11 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 93241502 EMBASE
DOCUMENT NUMBER: 1993241502
TITLE: Gel retardation analysis of E.Coli M1 RNA - tRNA complexes.
AUTHOR: Hardt W.-D.; Schlegl J.; Erdmann V.A.; Hartmann R.K.
CORPORATE SOURCE: Institut fur Biochemie, Freie Universitat Berlin, Thielallee 63,1000 Berlin 33, Germany
SOURCE: Nucleic Acids Research, (1993) 21/15 (3521-3527). ISSN: 0305-1048 CODEN: NARHAD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We have analyzed complexes between **tRNA** and E.coli M1 RNA by electrophoresis in non-denaturing polyacrylamide gels. The RNA subunit of E.coli RNase P formed a specific complex with mature **tRNA** molecules. A derivative of the **tRNA**(Gly), endowed with the intron of yeast **tRNA**(IIe) (60 nt), was employed to improve separation of complexed and unbound M1 RNA. **Binding** assays with **tRNA**(Gly) and intron-**tRNA**(Gly) as well as analysis of intron-**tRNA**/M1 RNA complexes on denaturing gels showed that one **tRNA** is **bound** per molecule of M1 RNA. A **tRNA** carrying a truncation as small as the 5'-nucleotide had a strongly reduced affinity to M1 RNA and was also a weak competitor in the cleavage reaction, suggesting that nucleotide + 1 is a major determinant of **tRNA** recognition and that the thermodynamically stable **tRNA**-M1 RNA complex is relevant for enzyme function. **Binding** was shown to be dependent on the M1 RNA concentration in a cooperative fashion. Only a fraction of M1 RNAs (50 - 60%) readily formed a complex with intron-**tRNA**(Gly), indicating that distinct conformational subpopulations of M1 RNA may exist. Formation of the M1 RNA-**tRNA**(Gly) complex was very similar at 100 mM Mg++ and Ca++, corroborating earlier data that Ca++ is competent in promoting M1 RNA folding and **tRNA binding**. Determination of apparent equilibrium constants (app Kd) for **tRNA**(Gly) as a function of the Mg++ concentration supports an uptake of at least two additional Mg++ ions upon complex formation. At 20 - 30 mM Mg++, highest cleavage rates but strongly reduced complex formation were observed. This indicates that tight **binding** of the **tRNA** to the **catalytic RNA** at higher magnesium concentrations retards product release and therefore substrate turnover.

L6 ANSWER 10 OF 11 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 1999:557818 SCISEARCH
THE GENUINE ARTICLE: 215KD
TITLE: The origin of the genetic code - amino acids as cofactors

in an RNA world
AUTHOR: Szathmary E (Reprint)
CORPORATE SOURCE: LORAND EOTVOS UNIV, DEPT PLANT TAXONOMY & ECOL, SZENTHAROMSAG U 2, H-1014 BUDAPEST, HUNGARY (Reprint); COLL BUDAPEST, H-1014 BUDAPEST, HUNGARY
COUNTRY OF AUTHOR: HUNGARY
SOURCE: TRENDS IN GENETICS, (**JUN 1999**) Vol. 15, No. 6, pp. 223-229.
Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.
ISSN: 0168-9525.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 64

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The genetic code, understood as the specific assignment of amino acids to nucleotide triplets, might have preceded the existence of translation. Amino acids became utilized as cofactors by **ribozymes** in a metabolically complex RNA world. Specific charging **ribozymes** **linked** amino acids to corresponding RNA handles, which could basepair with different **ribozymes**, via an anticodon hairpin, and so deliver the cofactor to the **ribozyme**. Growing of the 'handle' into a presumptive **tRNA** was possible while function was retained and modified throughout. A stereochemical relation between some amino acids and cognate anticodons/codons is likely to have been important in the earliest assignments. Recent experimental findings, including selection for **ribozymes** catalyzing peptide-bond formation and those utilizing an amino acid cofactor, hold promise that scenarios of this major transition can be tested.

L6 ANSWER 11 OF 11 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 97:180885 SCISEARCH
THE GENUINE ARTICLE: WK196
TITLE: Characterization of Neurospora mitochondrial group I introns reveals different CYT-18 dependent and independent splicing strategies and an alternative 3' splice site for an intron ORF
AUTHOR: Wallweber G J; Mohr S; Rennard R; Caprara M G; Lambowitz A M (Reprint)
CORPORATE SOURCE: OHIO STATE UNIV, DEPT MOL GENET, 484 W 12TH AVE, COLUMBUS, OH 43210 (Reprint); OHIO STATE UNIV, DEPT MOL GENET, COLUMBUS, OH 43210; OHIO STATE UNIV, DEPT BIOCHEM, COLUMBUS, OH 43210; OHIO STATE UNIV, DEPT BIOCHEM MED, COLUMBUS, OH 43210
COUNTRY OF AUTHOR: USA
SOURCE: RNA-A PUBLICATION OF THE RNA SOCIETY, (**FEB 1997**) Vol. 3, No. 2, pp. 114-131.
Publisher: CAMBRIDGE UNIV PRESS, 40 WEST 20TH STREET, NEW YORK, NY 10011-4211.
ISSN: 1355-8382.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 43

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The Neurospora crassa mitochondrial tyrosyl-**tRNA** synthetase (CYT-18 protein) functions in splicing the N. crassa mitochondrial large rRNA intron by stabilizing the catalytically active structure of the intron core. Here, a comprehensive study of N. crassa mtDNA group I introns identified two additional introns, cob-I2 and the ND1 intron, that are dependent on CYT-18 for splicing in vitro and in vivo. The other seven N. crassa mtDNA group I introns are not CYT-18-dependent and include five

that self-splice and two that do not splice under any conditions examined. Some of these introns may require maturases or other proteins for efficient splicing. AII but one of the non-CYT-18-dependent introns contain large peripheral extensions of the P5 stem, related to the P5abc structure that blocks CYT-18 **binding** to the Tetrahymena large rRNA intron. The remaining non-CYT-18-dependent intron, cob-zI1 contains a long, peripheral extension of the P9 stem, denoted P9.1, which also impedes CYT-18 **binding**. Detailed analysis of the CYT-18-dependent ND1 intron showed that two 3' splice sites are used in vitro and in vivo. The proximal, alternative 3' splice site brings the intron open reading frame, which potentially encodes a mobility **endonuclease**, in frame with the upstream exon, possibly providing a means of expression. Considered together, our results show that group I introns in N. crassa mitochondria use a variety of strategies involving different proteins and/or RNA structures to assist splicing, and they support the hypothesis that CYT-18 and the peripheral RNA structure P5abc are alternative evolutionary adaptations for stabilizing the active structure of the intron core.

```
=>
=> d his

     (FILE 'HOME' ENTERED AT 13:05:41 ON 13 MAY 2004)

     FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 13:05:52 ON 13
     MAY 2004
L1         92137 S TRNA?
L2        139414 S (ENZYMATI? NUCLE? ACID?) OR (CATALYT? RNA) OR (ENZYMAT? RNA)
L3           463 S L1 (S) (LINK? OR BOUND? OR BIND? OR CONJUG? OR TETHER? OR ATT
L4            40 S L3 AND AMINOACYL?
L5            22 DUP REM L4 (18 DUPLICATES REMOVED)
L6            11 S L5 AND PY<=2000

=> s (synthes? (3n) (polypepti or protei?)) and ((amino acid) (2n) ((non (n)
(nativ? or natura?) or synthet?)
UNMATCHED LEFT PARENTHESIS '2A) ((NON'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s (synthes? (3n) (polypepti or protei?)) and ((amino acid) (2n) ((non (n)
(nativ? or natura?) or synthet?))
UNMATCHED LEFT PARENTHESIS 'AND ((AMINO'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s (synthes? (3n) (polypepti or protei?)) and ((amino acid) (2n) ((non (n)
(nativ? or natura?) or synthet?)))
   3 FILES SEARCHED...
L7           348 (SYNTHES? (3N) (POLYPEPTI OR PROTEI?)) AND ((AMINO ACID) (2N)
                 ((NON (N) (NATIV? OR NATURA?) OR SYNTHET?)))

=> s l7 and trna
L8           122 L7 AND TRNA

=> s l8 and 2
L9            18 L8 AND 2

=> s l8 and l2
L10            8 L8 AND L2

=> dup rem l10
PROCESSING COMPLETED FOR L10
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L11           5 DUP REM L10 (3 DUPLICATES REMOVED)

=> s SUGA, h?/au; kourouklis, D?/au;  saito, H?/au; lee, n?/au; bonzagni, n?/au
L12        2780 SUGA, H?/AU


KOUROUKLIS, IS NOT A RECOGNIZED COMMAND
COMMAND STACK INTERRUPTED.  ENTER "DISPLAY HISTORY"
TO SEE WHICH COMMANDS WERE EXECUTED.

The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s SUGA, h?/au; s kourouklis, D?/au;s saito, H?/au;s lee, n?/au;s bonzagni, n?/au
L13        2780 SUGA, H?/AU


L14           7 KOUROUKLIS, D?/AU


L15       27128 SAITO, H?/AU


L16        7626 LEE, N?/AU


L17          23 BONZAGNI, N?/AU

=> s l13 or l14 or l15 or l16 or l17
L18       37502 L13 OR L14 OR L15 OR L16 OR L17

=> d his

     (FILE 'HOME' ENTERED AT 13:05:41 ON 13 MAY 2004)

     FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 13:05:52 ON 13
     MAY 2004
L1         92137 S TRNA?
L2        139414 S (ENZYMATI? NUCLE? ACID?) OR (CATALYT? RNA) OR (ENZYMAT? RNA)
L3           463 S L1 (S) (LINK? OR BOUND? OR BIND? OR CONJUG? OR TETHER? OR ATT
L4            40 S L3 AND AMINOACYL?
L5            22 DUP REM L4 (18 DUPLICATES REMOVED)
L6            11 S L5 AND PY<=2000
L7           348 S (SYNTHES? (3N) (POLYPEPTI OR PROTEI?)) AND ((AMINO ACID) (2N)
L8           122 S L7 AND TRNA
L9            18 S L8 AND 2
L10            8 S L8 AND L2
L11            5 DUP REM L10 (3 DUPLICATES REMOVED)
L12         2780 S SUGA, H?/AU
L13         2780 S SUGA, H?/AU
L14            7 S KOUROUKLIS, D?/AU
L15        27128 S SAITO, H?/AU
L16         7626 S LEE, N?/AU
L17           23 S BONZAGNI, N?/AU
L18        37502 S L13 OR L14 OR L15 OR L16 OR L17

=> d l18 and l2
L2 IS NOT VALID HERE
For an explanation, enter "HELP DISPLAY".

=> s l18 and l2
L19          341 L18 AND L2
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=> s l7 and l19
L20           0 L7 AND L19

=> s l7 and l18
L21           0 L7 AND L18

=> s l9 and trna
L22          18 L9 AND TRNA

=> dup rem l22
PROCESSING COMPLETED FOR L22
L23          17 DUP REM L22 (1 DUPLICATE REMOVED)

=> s l23 and py<=2000
   2 FILES SEARCHED...
L24          11 L23 AND PY<=2000

=> s l11 or l24
L25          16 L11 OR L24

=> d l25 1-16 ibib abs

L25  ANSWER 1 OF 16      MEDLINE on STN
ACCESSION NUMBER:    2002708903      MEDLINE
DOCUMENT NUMBER:     PubMed ID: 12470735
TITLE:               Incorporation of non-natural
                     amino acids into proteins.
AUTHOR:              Hohsaka Takahiro; Sisido Masahiko
CORPORATE SOURCE:    Department of Bioscience and Biotechnology, Okayama
                     University, 3-1-1 Tsushimanaka, 700-8530, Okayama, Japan.
SOURCE:              Current opinion in chemical biology, (2002 Dec) 6 (6)
                     809-15.  Ref: 42
                     Journal code: 9811312. ISSN: 1367-5931.
PUB. COUNTRY:        England: United Kingdom
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
                     General Review; (REVIEW)
                     (REVIEW LITERATURE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200306
ENTRY DATE:          Entered STN: 20021217
                     Last Updated on STN: 20030604
                     Entered Medline: 20030603
AB   Chemical and biological diversity of protein structures and functions can
     be widely expanded by position-specific incorporation of non-
     natural amino acids carrying a variety of
     specialty side groups.  After the pioneering works of Schultz's group and
     Chamberlin's group in 1989, noticeable progress has been made in expanding
     types of amino acids, in finding novel methods of tRNA
     aminoacylation and in extending genetic codes for directing the positions.
     Aminoacylation of tRNA with non-natural
     amino acids has been achieved by directed evolution of
     aminoacyl-tRNA synthetases or some ribozymes.  Codons
     have been extended to include four-base codons or non-natural base pairs.
     Multiple incorporation of different non-natural
     amino acids has been achieved by the use of a different
     four-base codon for each tRNA.  The combination of these novel
     techniques has opened the possibility of synthesising
     non-natural mutant proteins in living cells.

L25  ANSWER 2 OF 16      MEDLINE on STN
ACCESSION NUMBER:    2000017050      MEDLINE
```

DOCUMENT NUMBER: PubMed ID: 10549284
TITLE: Transfer RNA-dependent translocation of misactivated amino acids to prevent errors in **protein synthesis**.
AUTHOR: Nomanbhoy T K; Hendrickson T L; Schimmel P
CORPORATE SOURCE: Skaggs Institute for Chemical Biology, Scripps Research Institute, Beckman Center, La Jolla, California 92037, USA.
CONTRACT NUMBER: GM15539 (NIGMS)
SOURCE: Molecular cell, **(1999 Oct)** 4 (4) 519-28.
Journal code: 9802571. ISSN: 1097-2765.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991126

AB Misactivation of amino acids by aminoacyl-**tRNA** synthetases can lead to significant errors in **protein synthesis** that are prevented by editing reactions. As an example, discrete sites in isoleucyl-**tRNA synthetase** for **amino acid** activation and editing are about 25 A apart. The details of how misactivated valine is translocated from one site to the other are unknown. Here, we present a kinetic study in which a fluorescent probe is used to monitor translocation of misactivated valine from the active site to the editing site. Isoleucine-specific **tRNA**, and not other **tRNAs**, is essential for translocation of misactivated valine. Misactivation and translocation occur on the same enzyme molecule, with translocation being rate limiting for editing. These results illustrate a remarkable capacity for a specific **tRNA** to enhance amino acid fine structure recognition by triggering a unimolecular translocation event.

L25 ANSWER 3 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:37499 BIOSIS
DOCUMENT NUMBER: PREV200100037499
TITLE: A dual-specificity aminoacyl-**tRNA** synthetase in the deep-rooted eukaryote Giardia lamblia.
AUTHOR(S): Bunjun, Shipra; Stathopoulos, Constantinos; Graham, David; Min, Bokkee; Kitabatake, Makoto; Wang, Alice L.; Wang, Ching C.; Vivares, Christian P.; Weiss, Louis M.; Soll, Dieter [Reprint author]
CORPORATE SOURCE: Department of Molecular Biophysics and Biochemistry, Yale University, 266 Whitney Avenue, New Haven, CT, 06520-8114, USA
soll@trna.chem.yale.edu
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (November 21, 2000) Vol. 97, No. 24, pp. 12997-13002. print.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jan 2001
Last Updated on STN: 12 Feb 2002

AB Cysteinyl-**tRNA** (Cys-**tRNA**) is essential for **protein synthesis**. In most organisms the enzyme responsible for the formation of Cys-**tRNA** is cysteinyl-**tRNA** synthetase (CysRS). The only known exceptions are the euryarchaea Methanococcus jannaschii and Methanobacterium thermoautotrophicum, which do not encode a CysRS. Deviating from the accepted concept of one aminoacyl-**tRNA synthetase** per **amino acid**, these organisms employ prolyl-**tRNA**

synthetase as the enzyme that carries out Cys-**tRNA** formation. To date this dual-specificity prolyl-cysteinyl-**tRNA** synthetase (ProCysRS) is only known to exist in archaea. Analysis of the preliminary genomic sequence of the primitive eukaryote Giardia lamblia indicated the presence of an archaeal prolyl-**tRNA** synthetase (ProRS). Its proS gene was cloned and the gene product overexpressed in Escherichia coli. By using G. lamblia, M. jannaschii, or E. coli **tRNA** as substrate, this ProRS was able to form Cys-**tRNA** and Pro-**tRNA** in vitro. Cys-AMP formation, but not Pro-AMP synthesis, was **tRNA**-dependent. The in vitro data were confirmed in vivo, as the cloned G. lamblia proS gene was able to complement a temperature-sensitive E. coli cysS strain. Inhibition studies of CysRS activity with proline analogs (thiaproline and 5'-O-(N-(L-prolyl)-sulfamoyl)adenosine) in a Giardia S-100 extract predicted that the organism also contains a canonical CysRS. This prediction was confirmed by cloning and analysis of the corresponding cysS gene. Like a number of archaea, Giardia contains two enzymes, ProCysRS and CysRS, for Cys-**tRNA** formation. In contrast, the purified Saccharomyces cerevisiae and E. coli ProRS enzymes were unable to form Cys-**tRNA** under these conditions. Thus, the dual specificity is restricted to the archaeal genre of ProRS. G. lamblia's archaeal-type prolyl- and alanyl-**tRNA** synthetases refine our understanding of the evolution and interaction of archaeal and eukaryal translation systems.

L25 ANSWER 4 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1992:192849 BIOSIS
DOCUMENT NUMBER: PREV199293103799; BA93:103799
TITLE: CHARACTERIZATION OF THE REGULON CONTROLLED BY THE LEUCINE-RESPONSIVE REGULATORY PROTEIN IN ESCHERICHIA-COLI.
AUTHOR(S): ERNSTING B R [Reprint author]; ATKINSON M R; NINFA A J; MATTHEWS R G
CORPORATE SOURCE: BIOPHYSICS RES DIV, DEP BIOL CHEM, UNIVERSITY MICHIGAN, ANN ARBOR, MICHIGAN 48109, USA
SOURCE: Journal of Bacteriology, (1992) Vol. 174, No. 4, pp. 1109-1118.
CODEN: JOBAAY. ISSN: 0021-9193.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 13 Apr 1992
Last Updated on STN: 1 Jun 1992

AB The leucine-responsive regulatory protein (Lrp) has been shown to regulate, either positively or negatively, the transcription of several Escherichia coli genes in response to leucine. We have used two-dimensional gel electrophoresis to analyze the patterns of polypeptide expression in isogenic lrp+ and lrp mutant strains in the presence or absence of leucine. The absence of a functional Lrp protein alters the expression of at least 30 polypeptides. The expression of the majority of these polypeptides is not affected by the presence or absence of 10 mM exogenous leucine. Outer membrane porins OmpC and OmpF, glutamate synthetase (GlnA), the small sunit of glutamate synthase (GltD), lysyl-**tRNA** synthetase form II (LysU), a high-affinity periplasmic binding protein specific for branched-chain amino acids (LivJ), W protein, and the enzymes of the pathway converting threonine to glycine, namely, threonine dehydrogenase (Tdh) and **2**-amino-3-ketobutyrate coenzyme A ligase (Kbl), were identified as members of the Lrp regulon by electrophoretic analysis. We have shown that Lrp is a positive regulator of glutamate synthase and glutamine synthetase and that exogenous leucine has little or no effect on the expression of these proteins. In strains carrying a glnL detection and in strains carrying the glnL2302 allele, which directs the **synthesis** of a GlnL **protein** that is constitutively active, expression of glutamine synthetase is no longer regulated by Lrp, demonstrating that the effect of Lrp on glutamine

synthetase levels is indirect and requires an intact glnL gene. lrp::Tn10 strains grow poorly when arginine or ornithine is present as the sole nitrogen source in the medium. On the bases of present studies and previous research, we propose that Lrp is involved in the adaptation of E. coli cells to major shifts in environment, such as those which occur when E. coli leaves the intestinal tract of its animal host. Several genes required for amino acid and peptide transport and catabolism are negatively regulated by Lrp, and other genes required for amino acid biosynthesis and ammonia assimilation in a nitrogen-poor environment are positively regulated by Lrp.

L25 ANSWER 5 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1986:94843 BIOSIS
DOCUMENT NUMBER: PREV198681005259; BA81:5259
TITLE: CONTROL OF THE CELL-FREE **PROTEIN SYNTHESIS** BY AMINO-ACIDS EFFECTS ON TRANSFER RNA CHARGING.
AUTHOR(S): TYOBEKA E M [Reprint author]; MANCHESTER K L
CORPORATE SOURCE: DEP MED SCI, UNIV NORTH, SOVENGA 0727, S AFR
SOURCE: International Journal of Biochemistry, (1985) Vol. 17, No. 8, pp. 873-878.
CODEN: IJBOBV. ISSN: 0020-711X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 25 Apr 1986
Last Updated on STN: 25 Apr 1986

AB 1. In order to resolve the observation that addition of glutamine and glutamate appears to be of particular importance in enhancing the activity of a cell-free **protein synthesis** system derived from rat liver (Manchester and Tyobeka, 1980), we have measured the Km of the aminoacyl-**tRNA synthetases** towards **amino acids** and the extent of aminoacylation of **tRNA** under the conditions of our earlier experiments. **2**. During incubation of the cell-free system in the presence of an amino acid mixture the extent of acylation to **tRNA** of 15 amino acids studied showed no clear change from initial time values. 3. When incubation took place in the absence of added amino acids, however, the levels of glutamate and glutamine bound to their appropriate **tRNAs** dropped more rapidly and to lower levels than for other amino acids except tryptophan. 4. The pronounced drop for these two amino acids does not seem to result from an abnormally high Km value for the synthetases towards the respective amino acids, nor an abnormally low Vmax, but probably from the fact that the amounts of glutamyl and glutaminyl-**tRNA** in the cell-free system are comparatively low.

L25 ANSWER 6 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1977:203040 BIOSIS
DOCUMENT NUMBER: PREV197764025404; BA64:25404
TITLE: CELL-FREE HEMO GLOBIN SYNTHESIZING SYSTEMS FROM DEVELOPING CHICK EMBRYOS.
AUTHOR(S): HENDERSON A B; LEE J C
SOURCE: Texas Journal of Science Special Publication, (1976) No. 1, pp. 141-148.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable

AB From the onset of erythropoiesis through the 4th day of chick embryogenesis, **2** major species of Hb [embryonic (E) and primitive (P)] were present. Following the 4th day of development, **2** additional major species appeared [adult (A) and definitive (D)]. With further development (A + D)/(E + P) increased. Beyond the 17th day, E and P types were not detectable. To examine whether

translational control was involved in this differentiation, cell-free Hb synthesizing systems from the red blood cells of 4 and 17 day chick embryos were developed. The **protein synthesizing** components were separated into 3 fractions, salt-washed ribosomes, ribosome salt wash and a fraction containing **tRNA**, synthetases and elongation factors. Maximal incorporation of 3H-leucine into Hb by the systems required all 3 fractions in a well-defined ratio and Mg2+, K+, ATP, GTP, 19 other amino acids and an ATP generating system. Both the 4 and 17 day systems exhibited similar optimal [K+] and [ATP]/[Mg2+]. Both systems showed linear incorporation through 15 min of incubation and were capable of chain reinitiation. Products of the 17 day system were Hb of the A and D types by specific immunoprecipitation and by cochromatography on CM-Sephadex C-50. Approximately 90% of the incorporated radioactivity went into these Hb.

L25 ANSWER 7 OF 16 EMBASE
on STN

ACCESSION NUMBER: 92354447 EMBASE
DOCUMENT NUMBER: 1992354447
TITLE: Mutations activating the yeast eIF-**2**α kinase GCN2: Isolation of alleles altering the domain related to histidyl-**tRNA** synthetases.
AUTHOR: Ramirez M.; Wek R.C.; Vasquez de Aldana C.R.; Jackson B.M.; Freeman B.; Hinnebusch A.G.
CORPORATE SOURCE: Laboratory of Molecular Genetics, NICHHD, National Institutes of Health,Bethesda, MD 20892, United States
SOURCE: Molecular and Cellular Biology, (1992) 12/12 (5801-5815). ISSN: 0270-7306 CODEN: MCEBD4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The protein kinase GCN2 stimulates expression of the yeast transcriptional activator GCN4 at the translational level by phosphorylating the α subunit of translation initiation factor **2** (eIF-**2** α) in amino acid-starved cells. Phosphorylation of eIF- **2** α reduces its activity, allowing ribosomes to bypass short open reading frames present in the GCN4 mRNA leader and initiate translation at the GCN4 start codon. We describe here 17 dominant GCN2 mutations that lead to derepression of GCN4 expression in the absence of amino acid starvation. Seven of these GCN2(c) alleles map in the protein kinase moiety, and two in this group alter the presumed ATP-binding domain, suggesting that ATP binding is a regulated aspect of GCN2 function. Six GCN2(c) alleles map in a region related to histidyl-**tRNA** synthetases, and two in this group alter a sequence motif conserved among class II aminoacyl-**tRNA** synthetases that directly interacts with the acceptor stem of **tRNA**. These results support the idea that GCN2 kinase function is activated under starvation conditions by binding uncharged **tRNA** to the domain related to histidyl-**tRNA** synthetase. The remaining GCN2(c) alleles map at the extreme C terminus, a domain required for ribosome association of the protein. Representative mutations in each domain were shown to depend on the phosphorylation site in eIF-**2**α for their effects on GCN4 expression and to increase the level of eIF-**2**α phosphorylation in the absence of **amino acid** starvation. **Synthetic** GCN2(c) double mutations show greater derepression of GCN4 expression than the parental single mutations, and they have a slow- growth phenotype that we attribute to inhibition of general translation initiation. The phenotypes of the GCN2(c) alleles are dependent on GCN1 and GCN3, indicating that these two positive regulators of GCN4 expression mediate the inhibitory effects on translation initiation associated with

activation of the yeast eIF-2α kinase GCN2.

L25 ANSWER 8 OF 16 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 138:380506 CA
TITLE: Genes that are differentially expressed during erythropoiesis and their diagnostic and therapeutic uses
INVENTOR(S): Brissette, William H.; Neote, Kuldeep S.; Zagouras, Panayiotis; Zenke, Martin; Lemke, Britt; Hacker, Christine
PATENT ASSIGNEE(S): Pfizer Products Inc., USA; Max-Delbrueck-Centrum Fuer Molekulare Medizin
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003038130	A2	20030508	WO 2002-XA34888	20021031
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2003038130	A2	20030508	WO 2002-US34888	20021031
WO 2003038130	A3	20040212		
WO 2003038130	C1	20040422		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:
US 2001-335048P P 20011031
US 2001-335183P P 20011102
WO 2002-US34888 A 20021031

AB The present invention provides mol. targets that regulate erythropoiesis. Groups of genes or their encoded gene products comprise panels of the invention and may be used in therapeutic intervention, therapeutic agent screening, and in diagnostic methods for diseases and/or disorders of erythropoiesis. The panels were discovered using gene expression profiling of erythroid progenitors with Affymetrix HU6800 and HG-U95Av2 chips. Cells from an in vitro growth and differentiation system of SCF-Epo dependent human erythroid progenitors, E-cadherin+/CD36+ progenitors, cord blood, or CD34+ peripheral blood stem cells were analyzed. The HU6800 chip contains probes from 13,000 genes with a potential role in cell growth, proliferation, and differentiation and the HG-U95Av2 chip contains 12,000 full-length, functionally-characterized genes. [This abstract record is one of two records for this document

necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L25 ANSWER 9 OF 16 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 136:258038 CA
TITLE: Analysis of the chromosome sequence of the legume symbiont Sinorhizobium meliloti strain 1021
AUTHOR(S): Capela, Delphine; Barloy-Hubler, Frederique; Gouzy, Jerome; Bothe, Gordana; Ampe, Frederic; Batut, Jacques; Boistard, Pierre; Becker, Anke; Boutry, Marc; Cadieu, Edouard; Dreano, Stephane; Gloux, Stephanie; Godrie, Therese; Goffeau, Andre; Kahn, Daniel; Kiss, Erno; Lelaure, Valerie; Masuy, David; Pohl, Thomas; Portetelle, Daniel; Puhler, Alfred; Purnelle, Benedicte; Ramsperger, Ulf; Renard, Clotilde; Thebault, Patricia; Vandenbol, Micheline; Weidner, Stefan; Galibert, Francis
CORPORATE SOURCE: Laboratoire de Biologie Moleculaire des Relations Plantes-Microorganismes, Unite Mixte de Recherche (UMR) 215 Centre National de la Recherche Scientifique (CNRS), Institut National de la Recherche Agronomique, Chemin, Tolosan, F-31326, Fr.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(17), 9877-9882
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sinorhizobium meliloti is an α-proteobacterium that forms agronomically important N2-fixing root nodules in legumes. We report here the complete sequence of the largest constituent of its genome, a 62.7% GC-rich 3654,135-bp circular chromosome. Annotation allowed assignment of a function to 59% of the 3341 predicted protein-coding ORFs, the rest exhibiting partial, weak, or no similarity with any known sequence. Unexpectedly, the level of reiteration within this replicon is low, with only two genes duplicated with more than 90% nucleotide sequence identity, transposon elements accounting for 2.2% of the sequence, and a few hundred short repeated palindromic motifs (RIME1, RIME2, and C) widespread over the chromosome. Three regions with a significantly lower GC content are most likely of external origin. Detailed annotation revealed that this replicon contains all housekeeping genes except two essential genes that are located on pSymB. Amino acid/peptide transport and degradation and sugar metabolism appear as two major features of the S. meliloti chromosome. The presence in this replicon of a large number of nucleotide cyclases with a peculiar structure, as well as of genes homologous to virulence determinants of animal and plant pathogens, opens perspectives in the study of this bacterium both as a free-living soil microorganism and as a plant symbiont.
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 10 OF 16 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 135:133527 CA
TITLE: RNA-Catalyzed Amino Acid Activation
AUTHOR(S): Kumar, Raju K.; Yarus, Michael
CORPORATE SOURCE: Department of Molecular Cellular and Developmental Biology, University of Colorado, Boulder, CO, 80309-0347, USA
SOURCE: Biochemistry (2001), 40(24), 6998-7004
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have selected RNAs that perform a new reaction that chemical activates amino acids, paralleling mixed phosphate anhydride **synthesis** by **protein** aminoacyl-**tRNA** synthetases. Care with recovery of the unstable reaction product was apparently essential to this selection. The best characterized RNA, KK13, requires only Ca2+ for reaction and is optimally active at low pH with KM = 50 mM and kcat = 1.1 min-1 for activation of leucine. In conjunction with previous RNA-catalyzed aminoacyl-RNA synthesis, peptide bond formation, and RNA-based coding, these amino acid-activating RNAs complete an exptl. demonstration that the four fundamental reactions of protein biosynthesis can be RNA-mediated. The appearance of translation in an RNA world is therefore supported.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 11 OF 16 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 135:117662 CA

TITLE: Synthesis of non-natural mutants of λ-Cro repressor protein that contain an electron-accepting amino acid

AUTHOR(S): Sisido, Masahiko; Tokunaga, Shunsuke; Hohsaka, Takahiro

CORPORATE SOURCE: Department of Bioscience and Biotechnology, Faculty of Engineering, Okayama University, Okayama, 700-8530, Japan

SOURCE: Proceedings of the Japan Academy, Series B: Physical and Biological Sciences (**2000**), 76B(7), 92-96
CODEN: PJABDW; ISSN: 0386-2208

PUBLISHER: Nippon Gakushiin

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The protein biosynthetic system has been extended to incorporate **non-natural amino acids** in addition to the 20 naturally occurring ones. **TRNAs** were chemical aminoacylated with **non-natural amino acids** and the aminoacylated **tRNAs** were added to the cell lysate of E. coli, together with the target mRNA. The positions of the **non-natural amino acids** were directed by the 4-base codon/anticodon pairs that are orthogonal to the existing 3-base codon/anticodon pairs. Here, the position-specific incorporation of **non-natural amino acids** was applied to incorporate an electron-accepting amino acid, **2** -anthraquinonylalanine (anqAla) into a DNA-binding protein, λ-Cro repressor. The position of anqAla was directed by a CGGG 4-base codon introduced at several different positions on the mRNA. Among the several mutant proteins, the 64anqAla Cro showed a strong binding to the consensus double-stranded DNA.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 12 OF 16 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 118:164062 CA

TITLE: The mitochondrial tyrosyl-**tRNA** synthetase of Podospora anserina is a bifunctional enzyme active in **protein synthesis** and RNA splicing

AUTHOR(S): Kaemper, Ute; Kueck, Ulrich; Cherniack, Andrew D.; Lambowitz, Alan M.

CORPORATE SOURCE: Ruhr-Univ., Bochum, D-4630/1, Germany

SOURCE: Molecular and Cellular Biology (**1992**), 12(2), 499-511
CODEN: MCEBD4; ISSN: 0270-7306

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The Neurospora crassa mitochondrial tyrosyl-**tRNA** synthetase (mt tyrRS), which is encoded by the nuclear gene cyt-18, functions not only in aminoacylation but also in the splicing of group I introns. Here, the cognate P. anserina mt tyrRS gene, designated yts1, was isolated by using the N. crassa cyt-18 gene as a hybridization probe. DNA sequencing of the P. anserina gene revealed an open reading frame (ORF) of 641 amino acids which has significant similarity to other tyrRSs. The yts1 ORF is interrupted by two introns, one near its N terminus at the same position as the single intron in the cyt-18 gene and the other downstream in a region corresponding to the nucleotide-binding fold. The P. anserina yts1+ gene transformed the N. crassa cyt-18-**2** mutant at a high frequency and rescued both the splicing and **protein synthesis** defects. Furthermore, the YTS1 **protein synthesized** in Escherichia coli was capable of splicing the N. crassa mt large rRNA intron in vitro. Thus, YTS1 is a bifunctional protein active in both splicing and **protein synthesis**. The P. anserina YTS1 and N. crassa CYT-18 proteins share three blocks of amino acids that are not conserved in bacterial or yeast mt tyrRSs which do not function in splicing. One of these blocks corresponds to the idiosyncratic N-terminal domain shown previously to be required for splicing activity of the CYT-18 protein. The other two are located in the putative **tRNA**-binding domain toward the C terminus of the protein and also appear to be required for splicing. Since the E. coli and yeast mt tyrRSs do not function in splicing, the adaptation of the Neurospora and Podospora spp. mt tyrRSs to function in splicing most likely occurred after the divergence of their common ancestor from yeast.

L25 ANSWER 13 OF 16 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 112:94523 CA

TITLE: Homology of aspartyl- and lysyl-**tRNA** synthetases

AUTHOR(S): Gampel, Alexandra; Tzagoloff, Alexander

CORPORATE SOURCE: Dep. Biol. Sci., Columbia Univ., New York, NY, 10027, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1989**), 86(16), 6023-7
CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The yeast nuclear gene MSD1 coding for mitochondrial aspartyl-**tRNA** synthetase has been cloned and sequenced. The identity of the gene is confirmed by the following evidence. (1) The primary structure of the protein derived from the gene sequence is similar to that of the yeast cytoplasmic aspartyl-**tRNA** synthetase. (**2**) In situ disruption of MSD1 in a respiratory-competent haploid strain of yeast induces a pleiotropic phenotype consistent with a lesion in mitochondrial **protein synthesis**. (3) Mitochondria from a mutant with a disrupted chromosomal copy of MSD1 are unable to acylate mitochondrial aspartyl-**tRNA**. The primary structures of the cytoplasmic and mitochondrial aspartyl-**tRNA** synthetases are similar to the yeast cytoplasmic lysyl-**tRNA** synthetase, suggesting that the **2** types of synthetases may have a common evolutionary origin. Searches of the current protein banks also have revealed a high degree of sequence similarity of the lysyl-**tRNA** synthetase to the product of the Escherichia coli herC gene and to the partial sequence of a protein encoded by an unidentified reading frame located adjacent to the E. coli frdA gene. Based on the sequence similarities and the map positions of the herC and frdA loci, it is proposed that herC is the structural gene of the constitutively expressed lysyl-**tRNA** synthetase of E. coli and that the unidentified reading frame is the structural gene of the heat-inducible lysyl-**tRNA** synthetase.

L25 ANSWER 14 OF 16 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 91:137230 CA
TITLE: Influence of enol ether amino acids, inhibitors of ethylene biosynthesis, on aminoacyl transfer RNA synthetases and **protein synthesis**
AUTHOR(S): Mattoo, Autar K.; Anderson, James D.; Chalutz, Edo; Lieberman, Morris
CORPORATE SOURCE: Agric. Res., Sci. Educ. Adm., Beltsville, MD, 20705, USA
SOURCE: Plant Physiology (**1979**), 64(2), 289-92
CODEN: PLPHAY; ISSN: 0032-0889
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The analogs of rhizobitoxine, aminoethoxyvinylglycine (AVG) (L-**2**-amino-4-**2**'-aminoethoxy-trans-3 butenoic acid) and methoxyvinylglycine (MVG) (L-**2**-amino-4-methoxy-trans-3-butenoic acid), that are potent inhibitors of ethylene biosynthesis at 0.1 mM also inhibited **protein synthesis** and charging of **tRNA**, especially at ≥1 mM. The saturated analog of MVG inhibited ethylene synthesis, whereas the saturated analog of AVG did not. Both saturated AVG and MVG inhibited methionyl- and leucyl-amino acyl-**tRNA** synthetase. Because of the inhibition of amino acid metabolism in plant tissues by these rhizobitoxine analogs, caution is advised in interpreting the results obtained with concns. of compds. >0.1 mM.

L25 ANSWER 15 OF 16 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 66:72375 CA
TITLE: Mechanism of peptide bond formation in **protein synthesis**
AUTHOR(S): Schweet, Richard S.; Arlinghaus, Ralph B.; Heintz, Roger; Shaeffer, Joseph R.
CORPORATE SOURCE: Univ. of Kentucky Coll. of Med., Lexington, KY, USA
SOURCE: Collection of Papers presented at the Annual Symposium on Fundamental Cancer Research (**1965**), 19, 47-66
CODEN: SFCRAO; ISSN: 0097-2282
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Main topics reviewed and discussed are the translation of the hemoglobin messenger RNA (mRNA) and the transfer of amino acids from amino acyl-RNA. In new work studying peptide bond formation, ribosomes containing bound phenylalanine sRNA (phe-RNA) and free of GTP were incubated with the 2nd transfer enzyme (TF-**2**), peptide synthetase. About 25% of the phe-RNA was converted to polyphenylalanine-RNA (phephe-RNA). After hydrolysis, this became Phe-Phe. Evidence was obtained that the peptides were attached to transfer RNA while on the ribosome. This **tRNA** was the same as the original phe-RNA. It is suggested that the low yield of peptide is due to the small percentage of potentially active ribosomes which have **2** phe-RNA mols. bound. When the reaction mixture above is incubated with GTP, binding enzyme, and labeled phe-RNA, the amount of phe-RNA bound is greatly decreased and phephe-RNA and phe-phephe-RNA are increased. This change must be due to the addition of a single labeled phe-RNA, indicating that a considerable portion of the bound phe-RNA present after incubation with the binding enzyme and GTP is present as a single phe-RNA per ribosome. 52 references.

L25 ANSWER 16 OF 16 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 91:513825 SCISEARCH
THE GENUINE ARTICLE: GF101
TITLE: EVOLUTION AND RELATEDNESS IN **2** AMINOACYL-TRANSFER RNA-SYNTHETASE FAMILIES

AUTHOR: NAGEL G M (Reprint); DOOLITTLE R F
CORPORATE SOURCE: UNIV CALIF SAN DIEGO, CTR MOLEC GENET, M-034, LA JOLLA, CA, 92093 (Reprint); CALIF STATE UNIV FULLERTON, DEPT CHEM & BIOCHEM, FULLERTON, CA, 92634
COUNTRY OF AUTHOR: USA
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (**1991**) Vol. 88, No. 18, pp. 8121-8125.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 32

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Sequence segments of about 140 amino acids in length, each containing a selected consensus region, were used in alignments of the aminoacyl-**tRNA** synthetases with the aim of discerning their evolutionary relationships. In all cases tested, enzymes specific for the same amino acid from a variety of organisms grouped together, reinforcing the supposition that the aminoacyl-**tRNA** synthetases are very ancient enzymes that evolved to include the full complement of 20 amino acids long before the divergence leading to prokaryotes and eukaryotes. The enzymes are divided into two mutually exclusive groups that appear to have evolved from independent roots. Group I, for which two sequence segments were analyzed, contains the enzymes specific for glutamic acid, glutamine, tryptophan, tyrosine, valine, leucine, isoleucine, methionine, and arginine. Group II enzymes include those activating threonine, proline, serine, lysine, aspartic acid, asparagine, histidine, alanine, glycine, and phenylalanine. Both groups contain a spectrum of amino acid types, suggesting the possibility that each could have once supported an independent system for **protein synthesis**. Within each group, enzymes specific for chemically similar amino acids tend to cluster together, indicating that a major theme of synthetase evolution involved the adaptation of binding sites to accommodate related amino acids with subsequent specialization to a single amino acid. In a few cases, however, **synthetases** activating dissimilar **amino acids** are grouped together.

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=> s ribozyme? (2n) cataly? (2n) aminoacyl?
L26         16 RIBOZYME? (2N) CATALY? (2N) AMINOACYL?

=> dup rem l26
PROCESSING COMPLETED FOR L26
L27          8 DUP REM L26 (8 DUPLICATES REMOVED)

=> d his

     (FILE 'HOME' ENTERED AT 13:05:41 ON 13 MAY 2004)

     FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 13:05:52 ON 13
     MAY 2004
L1        92137 S TRNA?
L2       139414 S (ENZYMATI? NUCLE? ACID?) OR (CATALYT? RNA) OR (ENZYMAT? RNA)
L3          463 S L1 (S) (LINK? OR BOUND? OR BIND? OR CONJUG? OR TETHER? OR ATT
L4           40 S L3 AND AMINOACYL?
L5           22 DUP REM L4 (18 DUPLICATES REMOVED)
L6           11 S L5 AND PY<=2000
L7          348 S (SYNTHES? (3N) (POLYPEPTI OR PROTEI?)) AND ((AMINO ACID) (2N)
L8          122 S L7 AND TRNA
L9           18 S L8 AND 2
L10           8 S L8 AND L2
L11           5 DUP REM L10 (3 DUPLICATES REMOVED)
L12        2780 S SUGA, H?/AU
L13        2780 S SUGA, H?/AU
L14           7 S KOUROUKLIS, D?/AU
L15       27128 S SAITO, H?/AU
L16        7626 S LEE, N?/AU
L17          23 S BONZAGNI, N?/AU
L18       37502 S L13 OR L14 OR L15 OR L16 OR L17
L19         341 S L18 AND L2
L20           0 S L7 AND L19
L21           0 S L7 AND L18
L22          18 S L9 AND TRNA
L23          17 DUP REM L22 (1 DUPLICATE REMOVED)
L24          11 S L23 AND PY<=2000
L25          16 S L11 OR L24
L26          16 S RIBOZYME? (2N) CATALY? (2N) AMINOACYL?
L27           8 DUP REM L26 (8 DUPLICATES REMOVED)

=> s l27 not l25
L28           8 L27 NOT L25

=> d l27 1-8 ibib abs

L27  ANSWER 1 OF 8  CA  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         139:209953  CA
TITLE:                    Ribozymes with broad tRNA aminoacylation activity
INVENTOR(S):              Suga, Hiraoki; Murakami, Hiroshi; Saito, Hirohide
PATENT ASSIGNEE(S):       The Research Foundation of State University of New
                          York At Buffalo, USA
SOURCE:                   PCT Int. Appl., 85 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
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WO 2003070740 A1 20030828 WO 2003-US5007 20030218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2003228593 A1 20031211 US 2003-369036 20030218
PRIORITY APPLN. INFO.: US 2002-357424P P 20020215

AB The present invention provides catalytic RNA mols. having cis or trans aminoacylation activity. The catalytic RNA mols. having cis aminoacylation activity comprise a catalytic domain and an aminoacylation domain. The catalytic RNA mols. having trans aminoacylation activity only have the catalytic domain. A method is provided for constructing and screening of these mols. These mols. are suitable for aminoacylating with specific natural or non-natural amino acids. Thus, a ribozyme which charged tRNAAsn with phenylalanine analogs p-benzoyl-Phe and p-phenylazo-Phe was prepared One such ribozyme was immobilized and successfully used to aminoacylate tRNA. Suppressor tRNAs charged with Phe analogs using the above ribozyme were used in translation systems to prepare site-specifically mutated GFP.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 8 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:89815 CA
TITLE: Searching the origin of life by in vitro evolution system
AUTHOR(S): Saito, Hirohide; Watanabe, Kimitsuna; Suga, Hiroaki
CORPORATE SOURCE: Protein Prod. Res. Div., Japanese Found. Cancer Res., Japan
SOURCE: Tanpakushitsu Kakusan Koso (2002), 47(9), 1209-1214
CODEN: TAKKAJ; ISSN: 0039-9450
PUBLISHER: Kyoritsu Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review on the origin of life based on the RNA world hypothesis, the in vitro evolution system, ribozymes catalyzing RNA elongation (self-replication), important roles of ribozymes in origin of protein formation system, isolation of **ribozymes catalyzing aminoacylation** of tRNA (ARS-ribozyme) using in vitro evolution technique, and preparation of novel functional proteins using ARS-ribozyme.

L27 ANSWER 3 OF 8 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:212391 CA
TITLE: **Ribozyme-catalyzed** transfer RNA **aminoacylation**
AUTHOR(S): Lee, Nick
CORPORATE SOURCE: State Univ. of New York, Buffalo, NY, USA
SOURCE: (2001) 99 pp. Avail.: UMI, Order No. DA3021916 From: Diss. Abstr. Int., B 2002, 62(8), 3627
DOCUMENT TYPE: Dissertation
LANGUAGE: English

AB Unavailable

L27 ANSWER 4 OF 8 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 135:16031 CA
TITLE: Catalytic RNAs with aminoacylation activity and

application to aminoacylation of tRNA-like molecules
INVENTOR(S): Hiroaki, Suga; Dimitrios, Kourouklis; Hirohide, Saito; Lee, Nick; Bonzagni, Neil
PATENT ASSIGNEE(S): The Research Foundation of State University of New York, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001038582	A1	20010531	WO 2000-US32184	20001122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1232285	A1	20020821	EP 2000-982217	20001122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003514572	T2	20030422	JP 2001-539923	20001122

PRIORITY APPLN. INFO.: US 1999-167331P P 19991124
US 2000-214382P P 20000628
WO 2000-US32184 W 20001122

AB The present invention provides catalytic RNA mols. having cis or trans aminoacylation activity. The catalytic RNA mols. having cis aminoacylation activity comprise a catalytic domain and an aminoacylation domain. The catalytic RNA mols. having trans aminoacylation activity only have the catalytic domain. A method is provided for constructing and screening of these mols. These mols. are suitable for aminoacylating tRNA-like mols. with specific amino acids.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 5 OF 8 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001402531 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11453065
TITLE: A minihelix-loop RNA acts as a trans-aminoacylation catalyst.
AUTHOR: Lee N; Suga H
CORPORATE SOURCE: Department of Chemistry, State University of New York at Buffalo, 14260-3000, USA.
SOURCE: RNA (New York, N.Y.), (2001 Jul) 7 (7) 1043-51.
Journal code: 9509184. ISSN: 1355-8382.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010806
Last Updated on STN: 20010806
Entered Medline: 20010802

AB We previously reported a bifunctional **ribozyme** that **catalyzes** self-**aminoacylation** and subsequent acyl-transfer to a tRNA. The ribozyme selectively recognizes a biotinyl-glutamine substrate, and charges the tRNA molecule in trans.

Structurally, there are two catalytic domains, referred to as glutamine-recognition (QR) and acyl-transferase (ATRib). We report here the essential catalytic core of the QR domain as determined by extensive biochemical probing, mutation, and structural minimization. The minimal core of the QR domain is a 29-nt helix-loop RNA, which is also able to glutaminylate ATRib in trans. Its amino acid binding site is embedded in an 11-nt cluster that is adjacent to the loop that interacts with the ATRib domain. Our study shows that a minihelix-loop RNA can act as a trans-aminoacylation catalyst, which lends support for the critical role of minihelix-loops in the early evolution of the aminoacylation system.

L27 ANSWER 6 OF 8 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2000091079 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10625423
TITLE: **Ribozyme-catalyzed** tRNA **aminoacylation**.
COMMENT: Comment in: Nat Struct Biol. 2000 Jan;7(1):5-7. PubMed ID: 10625414
AUTHOR: Lee N; Bessho Y; Wei K; Szostak J W; Suga H
CORPORATE SOURCE: Department of Chemistry, State University of New York at Buffalo, Buffalo, New York 14260-3000, USA.
SOURCE: Nature structural biology, (2000 Jan) 7 (1) 28-33. Journal code: 9421566. ISSN: 1072-8368.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000131
Last Updated on STN: 20020121
Entered Medline: 20000118

AB The RNA world hypothesis implies that coded protein synthesis evolved from a set of ribozyme catalyzed acyl-transfer reactions, including those of aminoacyl-tRNA synthetase ribozymes. We report here that a bifunctional ribozyme generated by directed in vitro evolution can specifically recognize an activated glutaminyl ester and aminoacylate a targeted tRNA, via a covalent aminoacyl-ribozyme intermediate. The ribozyme consists of two distinct catalytic domains; one domain recognizes the glutamine substrate and self-aminoacylates its own 5'-hydroxyl group, and the other recognizes the tRNA and transfers the aminoacyl group to the 3'-end. The interaction of these domains results in a unique pseudoknotted structure, and the ribozyme requires a change in conformation to perform the sequential aminoacylation reactions. Our result supports the idea that aminoacyl-tRNA synthetase ribozymes could have played a key role in the evolution of the genetic code and RNA-directed translation.

L27 ANSWER 7 OF 8 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 128:305435 CA
TITLE: A novel ribozyme with ester transferase activity
AUTHOR(S): Jenne, Andreas; Famulok, Michael
CORPORATE SOURCE: Institut fur Biochemie der LMU Munchen-Genzentrum, Munchen, 81377, Germany
SOURCE: Chemistry & Biology (1998), 5(1), 23-34
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Current Biology Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The "RNA world" hypothesis proposes that the early history of life on earth consisted of a period in which chemical transformations were catalyzed exclusively by ribozymes. Ribozymes that act as acyl transferases, or catalyze the formation of amide or peptide bonds seem particularly attractive candidates to link the RNA world to the modern protein-nucleic acid world. The central role played by aminoacylated RNAs in today's

processes of translating RNA into protein suggests that aminoacyl transfer reactions catalyzed by RNA might have facilitated the development and optimization of the translation apparatus during early evolution. The authors describe the isolation and characterization of a novel ribozyme that catalyzes the transfer of an amino-acid ester from an aminoacyl donor substrate onto the ribozyme itself. The site of aminoacylation was determined to be at an internal 2'-OH group of a cytosine residue. The aminoacylation depends on the presence of Mg2+ and can be competitively inhibited by the AMP moiety of the aminoacyl donor substrate, suggesting that there is a specific binding pocket for this substrate. The originally selected ribozyme was engineered to act as an intermol. catalyst that transfers the amino acid onto an external 28-residue oligonucleotide. The aminoacylated oligonucleotide was further used to quantify the reverse reaction catalyzed by the ribozyme. The ribozyme the authors have isolated is an example of a catalytic RNA with ester transferase activity which uses a substrate that is not templated by Watson-Crick-pairing hydrogen bonds. The reaction catalyzed by the ribozyme expands the scope of RNA catalysis to include acyl transferase activity from an RNA 3' end to an internal 2' position and the reverse. Ribozymes with such activity have been postulated to be evolutionary precursors of rRNA.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 8 OF 8 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 122:234102 CA

TITLE: Aminoacyl-RNA synthesis catalyzed by an RNA

AUTHOR(S): Illangasekare, Mali; Sanchez, Giselle; Nickles, Tim; Yarus, Michael

CORPORATE SOURCE: Department of Molecular, Univ. of Colorado, Boulder, CO; 80309-0347, USA

SOURCE: Science (Washington, D. C.) (1995), 267(5198), 643-7 CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A catalytic RNA (ribozyme) was selected that rapidly aminoacylates its 2'(3')-terminus when provided with phenylalanyl-AMP. The RNA accelerated the same aminoacyl group transfer catalyzed by protein aminoacyl-tRNA synthetases. The best characterized RNA reaction required both Mg2+ and Ca2+. These results confirmed a necessary prediction of the RNA world hypothesis and represent efficient RNA reaction (≥105-fold accelerated) at a carbonyl C atom, exemplifying a little explored type of RNA catalysis.

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